representative of many situations where evaluation of the anatomy of the spleen is of importance in either diagnosis or treatment. Hereditary spherocytosis is usually satisfactorily controlled by splenectomy. Preoperative visualization of the spleen aids in confirming the diagnosis as well as in recognizing accessory spleens. Figures 1 and 2 show the clarity with which the spleens in these two cases were visualized. Multiple views are important to determine the size and position of the spleen. The left anterior oblique view most frequently visualizes the organ best.

The finding of splenomegaly at operation in these two patients with hereditary spherocytosis confirmed the value of this procedure as an aid in determining spleen size. Though it appears that the spleens were large enough to be found on physical examination alone, the patient's body habitus and the posterior position of the organ precluded this in these patients, suggesting the possibility that spleens of lesser size may be missed even more frequently. The ease and safety of the procedure further enhances the desirability of scintophotography as a diagnostic tool. For less enlarged spleens there are methods of predicting volume with reasonable accuracy although in obviously enlarged organs, such as these, visual examination alone is usually sufficient.

Summary

In two cases of hereditary spherocytosis splenomegaly was not discovered by physical or x-ray examination. Both patients were studied by scintiphotography, using ^{99m}Tc sulfur colloid as the spleen labeling agent. The finding of an enlarged spleen by this method in both patients was corroborated at the time of operation. These findings illustrate the value of this procedure.

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Myelography with Sodium Diatrizoate (Hypaque®)

Report of a Case of Inadvertent Use Complicated by Acute Renal Failure

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ALTHOUGH WATER-SOLUBLE contrast agents have been used for myelography, the pronounced toxicity and special precautions have brought these agents into disfavor in this country. Therefore for myelography or other procedures, direct intrathecal introduction of water-soluble contrast media is an infrequent occurrence.[1-8] However, in one previously reported case, a myelogram was performed with such an agent, and acute renal failure was a complication that followed. This paper reports another case of acute renal failure following myelogram performed with sodium diatrizoate. (Hypaque®)

Report of a Case

A 25-year-old Caucasian man was admitted to a hospital for evaluation of back pain after five days of lumbar traction. A myelogram was performed. Spinal fluid examination before the myelogram was normal. Fifteen milliliters of spinal fluid was removed and 5.0 ml of sodium diatrizoate was instilled into the subarachnoid space. This caused immediate but mild lower back and coccygeal pain radiating posteriorly into both thighs. After five minutes the pain spontaneously subsided. Another 3.0 ml of the same contrast medium were injected, again producing pain. The procedure was discontinued and the pain again quickly subsided. Two hours after the initial injection, severe pain recurred, associated with burning, paresthesias and pronounced spasm of the rectal, gluteal and anterior thigh muscles.

Over the next half hour the patient received 2.0 ml of dexamethasone, 1.0 ml of methapyrilene compound, 50 mg of meperidine hydrochloride, 25 mg of promazine hydrochloride, and 8.0 mg of morphine sulfate, all intramuscularly. This gave no relief of the severe muscle spasms, which had spread to involve the entire lower half of the

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body. Tonic-clonic seizure activity was observed and 15 gm of sodium amytal was given. Blood pressure fell from 125/80 to 90/30 mm of mercury. During the next hour, an additional 7.5 grams of sodium amytal, 2.0 ml of levarterenol bitartrate, 30 ml of dexamethasone, 50 mg of hydrocortisone sodium succinate, and 0.75 mg of digoxin were administered intravenously, and the patient was transferred to Tripler General Hospital.

On arrival, approximately five hours after the myelogram, he was semicomatose, responding only to painful stimuli. Blood pressure was 120/70 mm of mercury, pulse 80 per minute and temperature 37.5°C (100°F). Pupils were equal and reactive, and corneal and pharyngeal reflexes were present. Muscle tone was flaccid, but intermittently there was diffuse extensor spasm lasting 30 seconds. Deep tendon reflexes were symmetrical and hyperactive, and there were bilateral extensor plantar reflexes. The remainder of the physical examination was normal.

Leukocytes numbered 20,600 per cmm, with 93 percent neutrophils and 7 percent lymphocytes. The hematocrit was 42 percent and hemoglobin content was 14 grams per 100 ml of blood. Urinalysis showed many red blood cells but an otherwise normal sediment, and there was no proteinuria. Blood urea nitrogen (BUN) was 23 mg per 100 ml, serum glutamic oxaloacetic transaminase (SGOT) 1533 International units, and barbiturate level 3.0 mg per 100 ml. Serum haptoglobins were decidedly decreased (25 mg per 100 ml). The remainder of routine laboratory studies were normal.

Hospital course. The bladder was catheterized and 600 ml of dark, muddy brown urine were obtained. Spectrographic analysis showed the dark pigment in the urine to be methemoglobin. Lumbar puncture was done and the fluid was normal with a protein content of 24 mg per 100 ml. An electroencephalogram showed diffuse three-cycle-per-second waves. The patient became severely oliguric and was unresponsive to mannitol or furosemide. His semi-comatose state was attributed to barbiturate intoxication and possible encephalopathy secondary to the sodium diatrizoate. Pulse rate and blood pressure remained normal. He did not require intubation nor vasopressor therapy. There was no further seizure activity. Twelve hours after admission he was responsive to verbal command and could move all extremities. At the end of 24 hours he was fully alert and oriented but complained of low back pain radiating in a sciatic distribution and weakness of both legs. Progressive azotemia necessitated hemodialysis on four occasions over the next 14 days. Later he entered a diuretic phase and had complete recovery of renal function. Renal biopsy was not performed. Creatinine clearance at discharge was 140 ml per minute.

Because of persistent pain and weakness, a neurosurgical evaluation and electromyographic studies were obtained. These revealed no evidence of arachnoiditis, anterior horncell disease or peripheral neuropathy. Symptoms were felt to be secondary to neuralgia caused by sodium diatrizoate. After six weeks in hospitalization the patient still complained of mild back pain and posterior numbness of both thighs, but otherwise he had completely recovered.

Discussion

Several investigators[2,9-11] have demonstrated the pronounced toxicity of intrathecal sodium diatrizoate in animals, and its toxicity following similar injection in man is clearly stated in detailed literature accompanying the drug.

Of the 16 previously reported cases of accidental intrathecal administration of water-soluble contrast media, six were complications of discography, one was incident to a myelogram, one was from injection into a myelocele, and the remainder were complications of cerebral (seven cases) or translumbar (one case) angiograms. Four of the 16 patients died; 12 had complete recovery. The contrast media used were sodium diatrizoate (11 cases), iodopyracet (three cases), and Urografﬁn® (two cases). The volume of material administered ranged from 2 to 40 ml. It is not clear from the available data whether the type of contrast medium used related to the severity of the reaction. Symptoms do not seem to be entirely dose-related since there were two fatalities at small doses (6 and 8 ml) and two at large doses (30 and 40 ml). With the exception of the myelocele, the other three fatalities occurred in instances of cerebral vessel angiography where the contrast medium entered the high cervical or cisternal subarachnoid space. Thus, it appears that the proximity of the contrast medium to the intracranial subarachnoid space is as critical a factor in determining the severity and outcome as the dose of medium in-

jected. Similar observations were made by Praestholm and Lester[12] and this concept is also suggested in animal work by Hoppe and Archer[9] and Campbell et al.[10]

Clinically, a typical sequence is seen. Initially there is mild to severe, usually transient, pain in the area of injection. This is then followed frequently, but not always, by an asymptomatic period lasting from 30 minutes to two hours. Extreme pain, severe extensor spasms, hyperirritability and, in severe cases, convulsions may then develop. Both hypertension and hypotension have been initially noted. In severe cases, shock and apnea may ensue. In the reported fatal cases, death occurred within 2 to 4 hours; in the nonfatal cases, recovery was complete within 2 to 5 days.

Because of the potential seriousness of such accidents, treatment should be administered as soon as it is realized that water-soluble contrast medium has entered the subarachnoid space. Unfortunately, the treatment of this complication is not clearly established. Suggestions have included: elevating the head and shoulders to allow gravity flow toward the lumbar area;[2,5] lumbar puncture with removal of cerebro-spinal fluid, followed by cisternal puncture and irrigation of the subarachnoid space;[5] and sedation, usually in high doses, to control seizure activity. Corticosteroids, either systemically or intrathecally, have also been used. Other than basic supportive treatment, however, there is no evidence of the effectiveness of any of these means of treatment.

The pathogenesis of the central nervous system manifestations of this unusual problem is not known. Direct irritation of spinal cord has been postulated by most observers; however, Fundquist and Obel[11] expressed belief that the injurious effects may result from the hypertonicity of the contrast medium, rather than from a specific toxic action. The few post-mortem studies reported[2,8] have demonstrated no significant or specific central nervous system changes.

The cause of the acute renal failure in both the present case, as in that reported by Turner et al,[1] remains unclear. In both cases there was evidence of probable intravascular hemolysis and in both cases dark, muddy brown urine was noted. The urinary pigment was not identified by Turner et al, but in the case here reported it was found to be methemoglobin. We have no data to indicate whether the methemoglobin was filtered through the glomerular membrane or formed in the urine, although the decreased plasma haptoglobin levels suggest that there was intravascular hemolysis. It has been shown in experimental animals that methemoglobin is a more potent chemical inducer of acute renal failure than mercury.[13] The patient in the present case also had pronounced hypotension and received treatment with a potent vasoconstrictor, which may well have contributed to the acute renal failure.

Summary

A 25-year-old Caucasian man was admitted to hospital in semicomatose condition five hours after a myelogram had been administered with sodium diatrizoate, a water-soluble contrast agent considered decidedly toxic and therefore not held in favor for such use in the United States. The patient had neuralgia, also caused apparently by the sodium diatrizoate, and acute renal failure which necessitated hemodialysis on four occasions in a period of 14 days. After six weeks in hospital he still complained of mild back pain and numbness in both thighs posteriorly, but was otherwise completely recovered. Although the acute renal failure is not etiologically clear, the potent vasoconstrictor which the patient had received before arrival at the hospital may have well contributed to the condition.

TRADE AND GENERIC NAMES OF DRUGS

Hypaque® ..... sodium diatrizoate

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